INVENTOR: McBride et al
TITLE: MEDICAL TESTING AND METHOD

attorney docket: CARDIOBEAT-1

EXHIBIT 4

Answers to questions regarding Impedance Cardiography

Acceptance:

Impedance has not been widely accepted because its biophysics is not well investigated and the factors involved in the production of the signal are multiple and poorly understood. Impedance began to be promising about the same time that cardiac ultrasound came onto the scene. The physics of sonar was well researched; the technology proliferated rapidly and was marketed by many startup companies in the private sector. Virtually all of the research on impedance cardiography was done for the Apollo space flight by a team of researchers under Dr. William Kubicek, a physiologist at the University of Minnesota. The University held the patents on the device as the Minnesota Impedance Cardiograph. Like most universities, it was a disinterested entrepreneur, absent motivation from extensive clinical testing the technology languished. Computer power had to increase sufficiently to detect and assemble the average by separating the wandering "dirty" signal from cardiac impedance. Until the computing power was available, impedance would be seriously handicapped when comparing values against the "gold standard" for measuring cardiac output - measure the average of multiple cardiac cycles collected over a period of multiple seconds to minutes. Because it's accuracy was in question, and all of the gold standards for measuring cardiac output were invasive and thus not applicable to day to day monitoring any place but the intensive care unit, there was no precedent for it's use in the outpatient clinic setting .The medical community is conservative in embracing new ideas especially those not completely understood and explained by "hard " science facts and principles. Of course the electrocardiogram is still not completely explained and understood by hard science biophysics, but its utility has been accepted and validated through extensive clinical correlation and research, and even now new insights are gained annually about the electrocardiogram.

Except for a few of us, there is little clinical experience with this technology and therefore the opportunity for, and participation in, experience with the technology must occur before widespread acceptance can follow.

This is where a research partnership with a few large hospitals could be helpful. To validate the technology requires correlation with invasive measurements and one large group that almost always gets monitored early post operatively are coronary bypass patients and heart surgery patients in general. Invasive monitoring lines are removed as early as possible to reduce the risk of infection, but if a noninvasive technique can be shown to be reasonably accurate, safe and cheaper than the Invasive one, every hospital administrator in the country providing cardiac surgery and cardiac care services will want to pursue the more cost effective strategy. Considering the substantial costs of invasive monitoring and the affordable cost of impedance, the technique could be extended to cardiac rehabilitation and out patient heart failure monitoring and management. Congestive heart failure (CHF) is the most costly DRG for Medicare and is projected to expand almost exponentially in our aging population over the next 3 decades. The opportunity to substantially reduce the number of costly hospitalizations in the ever growing heart failure population and its economic impact on business government and society cannot be under estimated. I firmly believe that CHF is so much better treated with outpatient impedance directed therapy than with the typical inpatient course of care that only under extreme conditions such as sepsis or malignant arrhythmias should a patient with CHF be admitted to hospital. CHF is not a disease requiring hospitalization for it's optimum management. The disease must be managed in

the day to day environment where the patient lives. The strict diet, activity, and fluid restriction of the hospital environment only works until the patient leaves to go home, but is not applicable once he gets home, so he gets into trouble a little later and back he comes for another round of expensive care in the "ivory tower". Accurate, scheduled, hemo-dynamic surveillance can detect impending deterioration and direct appropriate treatment before the patient's condition reaches crisis proportions.

2) Demand and pricing:
The formula you used is right. If its' accuracy is valid then it's utility should be able to be proven. If it is perceived to have utility, widespread usage is inversely proportional to price.

What we are considering is a new paradigm for "medical technology business" where the profit has traditionally been made from selling the machine or "hardware". The new model is service or software analogous in that the machinery is viewed as a linkage device decreasing in purchase price all the time while ISP's underwrite the hardware purchase to get consumers tied to long-term service agreements. Digital satellite dishes, cell phones, digital pagers, and essentially all new age machinery are useless without service providers. Hell, even your car has OBD so you can't tune it without special software in the hands of a select few service providers.

Jim Buell 9-18-99